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This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided in Section 2150.

See reverse side for Additional information.

Interagency Report Control No. 0140-0036-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

FY 2006
ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. REGISTRATION NO. 51-F-016 Cust. ID 441

FORM APPROVED OMB NO. 0549-0036

2. **HEADQUARTERS RESEARCH FACILITY** (Name and Address, as registered with USDA, include zip code)

National Institutes of Health
Deputy Director for Intramural Research
31 Center Drive (b)(2)High, (b)(7)(F)
Bethesda , MD 20892

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3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS (Sites)	
Composite includes: APF, CC, NCI, NEI, NHGRI, NHLBI, NIA, NIAAA, NIAID, NIAID (RML), NIAMS, NICHD, NIDA, NIDCD,	NIDCR, NIDDK, NIEHS, NIMH, NINDS, ORS, VRC

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS FORM 7023A)

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments or tests were conducted involving no pain, distress or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery or tests. (an explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report.)	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs	29	34	101	0	135
5. Cats	11	4	6	0	10
6. Guinea Pigs	12	1236	62	0	1298
7. Hamsters	3067	355	676	18	1049
8. Rabbits	17	624	751	0	1375
9. Non-human Primates	988	1394	815	0	2209
10. Sheep	51	40	17	0	57
11. Pigs	29	66	164	0	230
12. Other Farm Animals	--	--	--	--	--
Goats	0	0	0	0	0
Burro	0	0	0	0	0
Horses	0	0	0	0	0
Cattle	2	0	0	0	0
Chickens	1	0	0	0	0
Quail	10	0	0	0	0

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment and use of animals, including appropriate use of anesthetic and tranquilizing drugs prior to, during And following actual research, teaching, testing, surgery or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (ACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)
I certify that the above is true, correct and complete (7 U.S.C. Section 2143)

SI(b)(6), (6)(7)(C)	ITIONAL OFFICIAL (Type or print)	DATE SIGNED
		11/22/06

APHIS FORM 7023 (Replaces VS FORM 18-23 (OCT 88) which is obsolete)
(AUG 91)

required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided in Section 2150.

See reverse side for Additional information.

Interagency Report Control No. 0188-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

FY 2006

CONTINUATION SHEET FOR ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. **REGISTRATION NO.**
2. **51-F-016 Cust. ID 441**

FORM APPROVED
OMB NO. 0549-0036

3 **HEADQUARTERS RESEARCH FACILITY** (Name and Address, as registered with USDA, include zip code)

National Institutes of Health
Deputy Director for Intramural Research
31 Center Driv(b)(2)High, (b)(7)(F)
Bethesda , MD 20892

RECEIVED
NOV 2 4 2006

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS FORM 7023A)

A. Animals Covered By The Animal Welfare Regulations 12 &/OR 13 OTHER (List by Species)	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments or tests were conducted involving no pain, distress or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery or tests. (an explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report.)	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
12. Goose	0	0	0	0	0
Duck	0	0	0	0	0
13. Gerbils	2	14	0	0	14
Ferrets	0	0	4	68	72
Cotton Rats	2	128	0	0	128
Squirrels	209	366	0	0	366
Pigeons	12	0	0	0	0
Frogs	659	1808	0	0	1808
Fish	0	0	0	0	122978
Other Amphibians	63	40	0	0	40
Vole	0	0	0	0	0
Mink	0	0	0	0	0
Wild Mice	57	4	0	0	4
Llama	1	0	0	0	0
Chinchillas	0	0	53	0	53

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment and use of animals, including appropriate use of anesthetic and tranquilizing drugs prior to, during And following actual research, teaching, testing, surgery or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)

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TIONAL OFFICIAL (Type or print)

DATE SIGNED
11/22/06

APHIS FORM 7023A
(AUG 91)

Column E Explanation Form

1. Registration Number: **51-F-0016**
2. Number of animals used under Column E conditions in this study. **68**
3. Species (common name) of animals used in this study. **ferrets**
4. Explain the procedure producing pain and/or distress, including reason(s) for species selected.

   The purpose of this project is to develop vaccines that protect humans against respiratory viruses, namely highly pathogenic avian influenza viruses. Viral infection and the induction of an immune response can only be studied in living animals. We were limited in our ability to study these viral infections and vaccine responses in the natural human host or a permissive primate model because of ethical considerations, limited availability, and limited genetic tools. Ferrets are mammalian models to study disease and evaluate potential vaccine candidates. Avian influenza viruses are not uniformly virulent for ferrets. Infection of ferrets with some highly pathogenic avian influenza viruses can result in disease symptoms that can range from very mild disease up to pneumonia and even, with no intervention, death. In this regard, it resembles the rare avian influenza infections reported in humans.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

   For the attenuation studies, we conducted studies to evaluate the level of attenuation of live vaccine candidates compared to the wild-type viruses that cause the disease in nature. H5N1 wild-type influenza viruses are shown to cause severe clinical signs in ferrets. Since the attenuation studies measure the ability of the virus to replicate in the animal, and some influenza virus subtypes cause clinical signs in ferrets, we did not administer antiviral agents or antipyretics/analgesics to animals that displayed clinical signs.

   The scientific justification for withholding anti-inflammatory drugs (NSAIDs) are as follows:

   Their use will inhibit the fever response and the fever response is an important endpoint for validating this model.

   The anti-inflammatory properties of the NSAID may affect the immune response to the viruses, which may affect the course of the disease.

The review by Aronoff and Neilson,(Am J Med 111: 304-315, 2001), reports that fever is tightly regulated by the immune response, is capable of countering the release of pyrogenic cytokines, and salicylates and other antipyretics suppress tissue inflammation. For these reasons, we did not administer antipyretics/analgesics to ferrets infected with influenza viruses.

EXPLANATION FOR COLUMN E LISTING

1. Registration Number: **51-F-0016**
2. 18 animals used under Column E conditions in this study: **FY 2005**
3. Species (common name) of animals used in this study: **Hamster**

4. Explain the procedure producing pain/or distress, including reason (s) for species selected.

Leishmanial diseases are major parasitic diseases of man. The stage of the parasite that grows in the vertebrate host and causes disease cannot be generated *in vitro*. It can only be obtained from *in vivo* sources. In nature, most leishmanial species are maintained within animal reservoirs, usually rodents. The hamster is the only laboratory animal that develops visceral leishmaniasis. There is no way to test the action of vaccines *in vitro*. The whole animal is required to study experimental vaccines, protective immune responses and the outcome of infection of vaccinated animals. Information derived from the immune system responses being examined cannot be gathered by using cell culture or computer models.
Visceral leishmaniasis in hamsters was manifested as hepatomegaly and anemia. The progression of visceral infection in hamsters was not associated with any overt pathology or changes in behavior until infection was severe, at which time hamsters began to move slowly and lose appetite.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

The point of onset of morbidity was variable, but it generally occurred in the period 12 - 16 weeks post infection (when parasite inoculum is low and parasites are injected intradermally). Without intervention, over several weeks, affected hamsters became cachectic and moribund.

The only means for pain or distress relief was euthanasia.

Analgesics were not used during the two-day period after morbidity was observed because they would affect the size, histology, and parasite load of infected organs. The consequences of which will affect endpoint comparative findings between vaccinated and non-vaccinated animals.

Those endpoint comparative findings are critical to the design of these studies the eventual identification of candidate vaccines.